UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,981	11/20/2001	Helen H. Hobbs	18781-007320	1693

20350 7590 08/08/2003

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER
NICHOLS, CHRISTOPHER J

ART UNIT	PAPER NUMBER
1647	11

DATE MAILED: 08/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/989,981	HOBBS ET AL.	
	Examin r	Art Unit	
	Christopher Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-70* is/are pending in the application.

4a) Of the above claim(s) *22-35 and 38-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21,36 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-21 and 36-37) drawn to an isolated nucleic acid molecule encoding an ABCG8 polypeptide, method for making said polypeptide, expression cassettes, and cell comprising same wherein said polypeptide is SEQ ID NO: 6 in Paper No. 10 (20 May 2003) is acknowledged.

2. The traversal is on the ground(s) that: (a) the search and examination of Groups I-VII and Groups A-H would not place a substantially greater burden on the Examiner, (b) Claim 1 is a generic claim with multiple species and the previous Office Action (Paper No. 8, 20 November 2002) does not follow the procedure set forth in 37 CFR §1.141-1.146 and the MPEP, (c) case law prohibits rejection of claims under 35 U.S.C. §121, (d) the Examiner denied the Applicant "the basic right of the applicant to claim his invention as he choose." *In re Weber*, 198 USPQ at 331, (e) Applicant reserves the right to petition the restriction requirement and appeal the rejections to the Board of Patent Appeals and Interferences (BPAI) pursuant to 37 C.F.R. §1.144.

3. The Applicant's traversal has been taken into full consideration and is not found persuasive for the following reasons. Firstly, each of the Groups as detailed in the Restriction Requirement (Paper No. 8, 20 November 2002) are independent and distinct thus requiring discrete and non-overlapping search and examination. On the grounds put forth in "(b)", that Claim 1 is a generic claim, the Examiner does not dispute that Claim 1 is a generic claim and the Applicant's argument is drawn to an election of species with regards to Markush practice. This is not the instant case. A second restriction requirement was made over the first because each sequence is an independent and distinct invention. Further 37 CFR §1.146 clearly states that:

"...the Examiner *may* require...", this is not compulsory and "...his or her claim will be restricted the if no claim to genus is found to be allowable." At the current time in the instant application's prosecution, no claims are allowable therefore restriction is permissible. The Examiner reminds the Applicant that upon allowance of a generic claim, rejoinder of withdrawn claims and inventions will be considered. Concerning "(c)", restriction is between inventions not claims. A single claim can encompass multiple inventions. Also, no rejection of any claims was set forth in the previous Office Action (Paper No. 8, 20 November 2002) under 35 U.S.C. §121, therefore the argument is not relevant. In regards to "(d)", the Examiner has not denied any rights of the Applicant in any way, shape, or form in respect to pursuing a patent on an invention as set forth in the previous Office Action (Paper No. 8, 20 November 2002). The Examiner has set forth the restriction requirement as to begin the search and examination process and as set forth in the previous Office Action, rejoinder will be considered upon reaching allowable subject matter. Finally, the Examiner accepts that the Applicant is free to petition the restriction requirement. However, the Examiner reminds the Applicant that no rejection of any claims was set forth in the previous Office Action (Paper No. 8, 20 November 2002) under 35 U.S.C. §121; therefore there are no rejections to appeal.

4. The Examiner notes, however, that upon completion of the art search for the instant application it has become evident that SEQ ID NO:'s 1, 2, 3, and 4 are linked together as murine sequences encoding ABCG5 and ABCG8 which interact to form a functional heterodimer and SEQ ID NO: 5, 6, 7, and 8 are like wise linked as human sequences {see Albrecht *et al.* (23 December 2002) "Functional analysis of candidate ABC transporter proteins for sitosterol transport." Biochimica et Biophysica Acta **1567**(1-2): 133-142}. Therefore, the Examiner has

hereby *withdrawn in part* the restriction requirement as set forth at pp. 5-6 ¶8-11 in the previous Office Action (Paper No. 8, 20 November 2002) to be TWO groups instead of EIGHT in the second restriction requirement as follows: Group X: SEQ ID NO: 1, 2, 3, 4 and Group Y: SEQ ID NO: 5, 6, 7, 8.

5. In addition, upon further consideration the election of species as set forth at pp. 6-7 ¶12-14 in the previous Office Action (Paper No. 8, 20 November 2002) is *withdrawn* such that if the withdrawn claims are rejoined upon allowance, no election of species will be imposed.

6. Claims 1-21 and 36-37 are under examination as drawn to the nucleic acid sequence SEQ ID NO: 5 which encodes the amino acid sequence SEQ ID NO: 6 and the nucleic acid sequence SEQ ID NO: 7 which encodes the amino acid sequence SEQ ID NO: 8. The Examiner has rejoined SEQ ID NO: 5, 6, 7, and 8 as to allow for search and examination of the elected invention in light of Applicant's election of SEQ ID NO: 6.

7. Claims 22-35 and 38-70 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant is reminded that upon reaching an allowable generic claim, rejoinder of withdrawn inventions will be taken into consideration. Applicant timely traversed the restriction (election) requirement in Paper No. 10 (20 May 2003).

8. The remaining restriction requirement is still deemed proper and is therefore made FINAL.

Status of Application, Amendments, and/or Claims

9. The Preliminary Amendments filed 21 February 2002 (Paper No. 3) and 23 July 2002 (Paper No. 6) have been received and entered in full.

Specification

10. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (pp. 23 line 8; pp. 69 line 5). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

11. Claims **1-21** and **36-37** objected to because of the following informalities: recite non-elected subject matter. Appropriate correction is required.

Provisional Obvious-Type Non-Statutory Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims **8-12** and **36-37** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-73 of U.S. Patent Application 2002/0081687 A1 (27 June 2002) Tian *et al.* Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of US 2002/0081687 are drawn to an amino acid sequence with 100% sequence homology to SEQ ID NO: 6 and SEQ ID NO: 5 thus meeting the limitations of claims 8-12 (Figures 7-9; Col. 28-42). The claims of US 2002/0081687 are also drawn to a recombinant method of making SSG polypeptides which share 100% sequence homology to SEQ ID NO: 6 thus meeting the limitations of claims 36 and 37 (paragraphs [0125]-[0174]). This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims **1-21** and **36-37** are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *nucleic acids comprising SEQ ID NO: 5 and SEQ ID NO; 7, expression cassettes, and host cells comprising same, and a method for making polypeptides comprising SEQ ID NO: 6 and SEQ ID NO: 8*, does not reasonably provide enablement for *nucleic acid or amino acid sequences which are 70% similar to SEQ ID NO: 5 or 6, expression cassettes, host cell comprising same, or methods of making polypeptides which are at least about*

70% similar to SEQ ID NO: 6 or 8. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

14. The claims are drawn very broadly to amino acid and nucleic acid sequences which share at least about 70% to SEQ ID NO: 6 and SEQ ID NO: 5. The language of said claims encompasses mutations, variants, derivatives, and fragments of said sequences.

15. The above invention is drawn to methods SEQ ID NO: 5 or 7, expression cassettes, host cells comprising same, and method of making a ABCG5 polypeptide recombinantely. The specification teaches that SEQ ID NO: 5 encodes SEQ ID NO: 6 which is ABCG5, a protein involved in cholesterol transport and sisterolemia. The specification teaches that SEQ ID NO: 7 encodes SEQ ID NO: 8 which is ABCG8, a protein involved in cholesterol transport and sisterolemia. ABCG5 and ABCG8 interact to form a functional heterodimer.

16. The specification fails to provide any guidance for the successful isolation and characterization of mutations, variants, derivatives, and fragments of said sequences, and since resolution of the various complications in regards to protein biochemistry highly unpredictable, one of skill in the art would have been unable to practice the invention without engaging in undue trial and error experimentation. In order to practice the invention using the specification and the state of the art as outlined below, the quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of mutations, variants, derivatives, and fragments of said sequences with known ABCG5 isoforms. In the absence of any guidance from the specification, the amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed.

17. Since the specification as filed does not provide any guidance or examples that would enable a skilled artisan to use the disclosed methods of using mutations, variants, derivatives, and fragments of said sequences to make a functional ABCG5 protein. Additionally, a person skilled in the art would recognize that predicting the efficacy of using a mutations, variants, derivatives, and fragments of said sequences based solely on sequence homology is highly problematic. Thus, although the specification prophetically considers and discloses general methodologies of using the claimed mutations, variants, derivatives, and fragments of said sequences, such a disclosure would not be considered enabling since the state of protein biochemistry is highly unpredictable. The factors listed below have been considered in the analysis of enablement:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

18. The following references are cited herein to illustrate the state of the art of ABCG and protein biochemistry.

19. On the breadth of the claims, Berge *et al.* (1 December 2000) "Accumulation of Dietary Cholesterol is Sitosterolemia Caused by Mutations in Adjacent ABC Transporters." Science **290**: 1771-1775 teach that singe bp changes in ABCG8 can cause sitosterolemia (Table1). It is noted that Berge *et al.* disclose sequences that share 100% sequence homology with SEQ ID NO: 5, 6,

and 8. Thus the breath of the claims is too broad to be fully enabled as even single bp changes can eliminate or lessen ABCG activity and thus not meet the full limitations of the claims.

20. On the nature of the invention, Lee *et al.* (April 2001) "Genetic Basis of sitosterolemia." Current Opinion in Lipidology **12**(2): 141-149 teaches that point mutations can lead to the development of sitosterolemia in humans (Table 1). Since claims 4, 5, 6, 18, and 19 are drawn to limitations based on the proper functioning of the ABCG dimer and normal, non-pathological expression and tissue specificity, it is not clear that a nucleic acid or polypeptide that is 70% homologous will retain the specific ABCG activity or expression and tissue patterns. Thus the skilled artisan is confronted with an undue burden of experimentation of trial and error to determine which nucleic acids and polypeptides that are at least 70% homologous to the claims SEQ ID NO's meet these limitations.

21. Concerning the predictability in the art, Graf *et al.* (September 2002) "Coexpression of ATP-binding cassette proteins ABCG5 and ABCG8 permits their transport to the apical surface." The Journal of Clinical Investigation **110**(5): 659-669 teaches that ABCG5 and ABCG8 form a functional heterodimer and may be required for successful post-translational modification and protein trafficking within the cell (pp. 660). Thus in light of the effects of mutations on the proteins, the skilled artisan can not predict how or if any variants of the claimed SEQ ID NO's can be successfully expressed.

22. Regarding derivatives and fragments of SEQ ID NO: 5, 6, 7, and 8, the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the

positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions [see Wells (18 September 1990) "Additivity of Mutational Effects in Proteins." Biochemistry **29**(37): 8509-8517; Ngo *et al.* (2 March 1995) "The Protein Folding Problem and Tertiary Structure Prediction, Chapter 14: Computational Complexity Protein Structure Prediction, and the Levinthal Paradox" pp. 492-495]. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone [Bork (2000) "Powers and Pitfalls in Sequence

Analysis: The 70% Hurdle." Genome Research **10**:398-400; Skolnick and Fetrow (2000) "From gene to protein structure and function: novel applications of computational approaches in the genomic era." Trends in Biotech. **18**(1): 34-39, especially p. 36 at Box 2; Doerks *et al.*, (June 1998) "Protein annotation: detective work for function prediction." Trends in Genetics **14**(6): 248-250; Smith and Zhang (November 1997) "The challenges of genome sequence annotation or 'The devil is in the details'." Nature Biotechnology **15**:1222-1223; Brenner (April 1999) "Errors in genome annotation." Trends in Genetics **15**(4): 132-133; Bork and Bairoch (October 1996) "Go hunting in sequence databases but watch out for the traps." Trends in Genetics **12**(10): 425-427]. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

23. Thus the specification of the instant application fails to provide adequate guidance for one of skill in the art to overcome the unpredictability and challenges of applying results from practicing the full scope of the invention relying solely on sequence homology as exemplified in the references herein.

24. Claims **1, 8, 12,** and **15** are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

25. The claims are drawn to polypeptides having at least 70% sequence identity with a particular disclosed sequence. The claims do not require that the polypeptide possess any particular conserved structure, or other distinguishing feature, such as a specific biological activity. Thus, the claims are drawn to a genus of polypeptides that is defined by sequence identity.

26. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claim that is sufficiently disclosed is a partial structure in the form of a recitation of percent identity. The specification does not identify any particular portion of the structure that must be conserved, nor does it provide a disclosure of structure/function correlation. The distinguishing characteristics of the claimed genus are not described. The only adequately described species is a polypeptide comprising SEQ ID NO: 6 or 8 or a nucleic acid comprising SEQ ID NO: 5 or 7. No active variants are disclosed. Accordingly, the specification does not provide adequate written description of the claimed genus.

27. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry,

whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

28. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

29. Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 6 and 8 and the nucleic acid sequence set forth in SEQ ID NO: 5 and 7, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

30. Claims **1-3, 13-16,** and **36-37** are rejected under 35 U.S.C. 102(e) as being anticipated by WO 02/40541 A2 (23 May 2002) Tang *et al.* WO 02/40541 teaches an amino acid sequence with 99.7% sequence homology to SEQ ID NO: 8 and 99.8% sequence homology with SEQ ID NO: 7 thus meeting the limitations of claims 1-3 and 13-16 (see sequence listing pp. 1-48). WO 02/40541 also teaches a method of recombinantly expressing said nucleic acid in an expression vector with a promoter as to produce a sequence with 99.7% sequence homology to SEQ ID NO: 8 thus meeting the limitations of claims 36 and 37 (claims 9 and 10).

31. Claims **8-12** and **36-37** are rejected under 35 U.S.C. 102(e) as being anticipated by WO 02/27016 A2 (4 April 2002) Patel *et al.* WO 02/27016 teaches an amino acid sequence with 100% sequence homology to SEQ ID NO: 6 and SEQ ID NO: 5 thus meeting the limitations of claims 8-12 (pp. 35-47). WO 02/27016 also teaches a method of recombinantly expressing said nucleic acid in an expression vector with a promoter as to produce a sequence with 100% sequence homology to SEQ ID NO: 6 thus meeting the limitations of claims 36 and 37 (claims 35-43; pp. 15-17).

32. Claims **8-12** and **36-37** are rejected under 35 U.S.C. 102(e) as being anticipated by WO 01/79272 A2 (25 October 2001) Tian *et al.* WO 01/79272 teaches an amino acid sequence with 100% sequence homology to SEQ ID NO: 6 and SEQ ID NO: 5 thus meeting the limitations of claims 8-12 (pp. 72-78). WO 01/79272 also teaches a method of recombinantly expressing said nucleic acid in an expression vector with a promoter as to produce a sequence with 100%

sequence homology to SEQ ID NO: 6 thus meeting the limitations of claims 36 and 37 (claims 1-18, 31-32; pp. 32-37).

Summary

33. Claims 1-21 and 36-37 are hereby rejected.

34. The following articles, patents, and patent publications were found by the Examiner during the art search and are here made of note:

a. US 2003/0027259 A1 (6 February 2003) Chen *et al.* {teaches a sequence with 100% sequence homology to SEQ ID NO: 6 and 99.9% sequence homology to SEQ ID NO: 8}

b. WO 01/79272 A2 (25 October 2001) Tian et al. {teaches a sequence with 100% sequence homology to SEQ ID NO: 6}

c. Salen *et al.* (2002) "Sitosterolemia." Cardiovascular Drug Reviews **20**(4): 255-270

d. Hubacek *et al.* (October 2001) "Mutations in ATP-cassette binding proteins G5 (ABCG5) and G8 (ABCG8) causing sitosterolemia." Hum Mutat. **18**(4): 359-360

e. Heimer *et al.* (August 2002) "Mutations in the human ATP-binding cassette transporters ABCG5 and ABCG8 in sitosterolemia." Hum Mutat. **20**(2): 151

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:00AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Gary Kunz, Ph.D.** can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

CJN
July 30, 2003

GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600